Public Health Service

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
555 Winderley Place, Suite 200
Maitland, Florida 32751

CERTIFIED LETTER
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-99-01

October 1, 1998

Dr. Thomas M. Riedhammer
President
Bausch and Lomb Pharmaceuticals, Inc.
8500 Hidden River Parkway
Tampa, Florida 33637

Dear Dr. Riedhammer:

During an inspection of your facility located in Tampa, Florida on July 27 through August 10, 1998, FDA Investigator Karen G. Hirshfield found serious deviations in the manufacture and distribution of the drug product, Neomycin and Polymyxin B Sulfates and Dexamethasone Ophthalmic Suspension USP (Sterile), which product is a human drug within the meaning of section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed that this drug is adulterated within the meaning of section 501(a)(2)(B) of the Act in that it is a drug product and the methods used in, or the facilities or controls used for, its manufacture, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice (GMP) regulations for drugs specified in Title 21 CFR, Part 211 as follows:

> The written procedures and process controls designed to assure that the product has the identity, strength, quality and purity it purports or is represented to possess are inadequate, in that they fail to assure the potency of Dexamethasone under ordinary and reasonable conditions of storage and use;

Failure to establish scientifically sound and appropriate product specifications, standards and test procedures for this product, to assure that components, containers, closures, and finished products conform to appropriate standards of identity, strength, quality and purity, in that they fail to take into account the different positions the product will be subject to under normal conditions of storage and use;

Failure to perform adequate validation studies on the container/closure system, component particle size, or content uniformity in the finished product container to assure that potency of the Dexamethasone will not be compromised by the collection of Dexamethasone in the container tip when held in a horizontal or inverted position.

We have received your response dated August 14, 1998, but do not believe that labeling the product "Store Upright" and "Shake Well Before Using" is a sufficient solution to the problem. Testing by your firm has shown that once the Dexamethasone has precipitated and settled into the tip, agitation alone will not resolve the problem. You also make reference to the innovator product, [redacted] but you have not run comparison studies to show that the two products have comparable problems. Further, Investigator Hirshfield discussed certain aspects of SOP 73-084, "Decision Path for Retesting", including definitions of what samples are applicable for retesting and when averaging is acceptable, third analyst testing, and the use of flow diagrams that allowed retesting until satisfactory results were achieved, which were not completely addressed in your response. Please include a discussion of any changes made to SOP 73-084 in these areas.

This letter is not intended to be an all-inclusive list of deficiencies at your facility, nor does it cover any issues other than those involving GMP's. It remains your responsibility to ensure adherence to all requirements of the Act and regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, any pending export approval requests may not be approved until the above violations are corrected.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct these violations and to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen working days, state the reason for the delay and the time within which corrections will be completed.

Your response should be sent to the Food and Drug Administration, Florida District Office, 555 Winderley Place, Ste. 200, Florida 32751, Attention: Martin E. Katz, Compliance Officer.

Sincerely,

Douglas D. Tolen
Director, Florida District

cc: C. Christine Simmons
VP, Regulatory Affairs

Eileen V. Farinacci-Perello
VP, Operations

Suzanne Martz
Director, Quality Assurance & Technical Services